BEST AVAILABLE COPY

BEST AVAILABLE COPY

Access DB# 558 18

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name:		Examiner #:	Date:	
Art Unit:	Phone Number 30	Serial Number:		
Mail Box and Bldg/Roon	n Location:	Examiner # : Serial Number: Results Format Preferred (circle):	PAPER DISK E-MAIL	
If more than one search	ı is submitted, please	prioritize searches in order of ne	ed. ********	
Include the elected species or	structures, keywords, synon; e any terms that may have a	I describe as specifically as possible the subj yms, acronyms, and registry numbers, and co special meaning. Give examples or relevant laims, and abstract.	ombine with the concept or	
Title of Invention:				
Earliest Priority Filing Da	ate:			
For Sequence Searches Only	Please include all pertinent in	formation (parent, child, divisional, or issued pa	tent numbers) along with the	

Jān Dēlāvāl Reference Librarian Biotechnology & Chemical Library CM1 1E07 – 703-308-4498 jan.delaval@uspto.gov

********	*******	**********
STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher:	NA Sequence (#)	STN
Searcher Phone #: 4198	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up: 3115 8	Bibliographic	Dr. Link
Date Completed: 3153	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time:	Other	Other (specify)
		;;' '

```
egin 5,73,155,399
       03may03 07:31:33 User208760 Session D2298.2
            $0.00
                    0.071 DialUnits File410
     $0.00 Estimated cost File410
     $0.03 TELNET
     $0.03 Estimated cost this search
     $0.35 Estimated total session cost
                                           0.161 DialUnits
SYSTEM:OS - DIALOG OneSearch
  File
       5:Biosis Previews(R)
                              1969-2003/Apr W4
         (c) 2003 BIOSIS
        5: Alert feature enhanced for multiple files, duplicates
*File
removal, customized scheduling. See HELP ALERT.
  File 73:EMBASE 1974-2003/Apr W4
         (c) 2003 Elsevier Science B.V.
*File 73: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File 155:MEDLINE(R) 1966-2003/Apr W4
         (c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have
changed. Please see HELP NEWS 155.
  File 399:CA SEARCH(R) 1967-2003/UD=13818
         (c) 2003 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
Alert feature enhanced for multiple files, etc. See HELP ALERT.
      Set Items Description
                 ______
          ----
? s (cd40L or cd40(w)ligand) and (treat? or therap? or prevent? or suppress? or
block? or inhibit?) (20n) (cancer? or tumor? or tumour?)
Processing
Processing
Processing
Processing
Processing
Processing
            4407 CD40L
           17518 CD40
          342860 LIGAND
            7980 CD40(W)LIGAND
         6000244 TREAT?
         5560564 THERAP?
         1926273 PREVENT?
          746765 SUPPRESS?
         1172882 BLOCK?
         3709658 INHIBIT?
         1990055 CANCER?
                 TUMOR?
         2021890
          268769
                  TUMOUR?
         1025598
                 (((((TREAT? OR THERAP?) OR PREVENT?) OR SUPPRESS?) OR
                  BLOCK?) OR INHIBIT?) (20N) ((CANCER? OR TUMOR?) OR TUMOUR?)
                  (CD40L OR CD40(W)LIGAND) AND (TREAT? OR THERAP? OR
      S1
             745
                  PREVENT? OR SUPPRESS? OR BLOCK? OR INHIBIT?) (20N) (CANCER?
                  OR TUMOR? OR TUMOUR?)
? s s1 and photodynamic
             745 S1
           26253 PHOTODYNAMIC
               1 S1 AND PHOTODYNAMIC
      S2
? t s2/3/all
           (Item 1 from file: 399)
 2/3/1
DIALOG(R) File 399:CA SEARCH(R)
(c) 2003 American Chemical Society. All rts. reserv.
```

```
CA: 135(24)339226q
                                     PATENT
  135339226
  Method for treatment of tumors using photodynamic therapy
  INVENTOR (AUTHOR): Fanslow, William C., III; Thomas, Elaine K.
  LOCATION: USA
  ASSIGNEE: Immunex Corporation
  PATENT: PCT International; WO 200180888 A2 DATE: 20011101
  APPLICATION: WO 2001US13616 (20010425) *US PV199545 (20000425)
  PAGES: 24 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A
 DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;
CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR;
HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA;
MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL;
TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD;
RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG
; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT;
SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
? s s1 and cd30?
             745
                 S1
            5966 CD30?
              33 S1 AND CD30?
      S3
? rd s3
...completed examining records
              25 RD S3 (unique items)
      S4
? t s4/3/all
 4/3/1
           (Item 1 from file: 5)
DIALOG(R) File
               5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.
13501169
           BIOSIS NO.: 200200129990
Depletion of normal B-lymphocytes by rituximab therapy alters serum
  cytokine levels, resolves B-symptoms and induces clinical remissions in
  patients with relapsed classical Hodgkin's disease (HD).
AUTHOR: Younes Anas(a); Romaguera Jorge(a); Hagemeister Frederick(a);
  Mclaughlin Peter(a); Rodriguez Maria Alma(a); Fiumara Paolo(a); Goy Andre
  (a); Jeha Sima; Manning John; Medeiros L Jeffrey; Martinez Rudy F(a);
  Cabanillas Fernando(a)
AUTHOR ADDRESS: (a) Lymphoma/Myeloma, M.D. Anderson Cancer Center (MDACC),
  Houston, TX**USA
JOURNAL: Blood 98 (11 Part 1):p132a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of
Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
 4/3/2
           (Item 2 from file: 5)
               5:Biosis Previews(R)
DIALOG(R) File
(c) 2003 BIOSIS. All rts. reserv.
          BIOSIS NO.: 200100320132
13112983
A pilot study of rituximab in patients with relapsed Hodgkin's disease of
  classical type.
AUTHOR: Younes A(a); Romaguera J(a); Hagemeister F(a); Rodriguez M(a);
  McLaughlin P(a); Medeiros J(a); Cabanillas F(a)
AUTHOR ADDRESS: (a) U.T. M.D. Anderson Cancer Center, Houston, TX**USA
JOURNAL: Blood 96 (11 Part 1):p733a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of
Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
```

RECORD TYPE: Abstract LANGUAGE: English SUMMARY LANGUAGE: English

4/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

13057538 BIOSIS NO.: 200100264687

Chronic lymphocytic leukemia B cells impair immunoglobulin class switching by inducing CD30+ suppressor T cells.

AUTHOR: Cerutti Andrea(a); Kim Edmund C(a); Zan Hong(a); Schaffer Andras(a); Casali Paolo(a)

AUTHOR ADDRESS: (a) Weill Medical College of Cornell University, 1300 York Avenue, New York, NY, 10021**USA

JOURNAL: FASEB Journal 15 (5):pA1202 March 8, 2001

MEDIUM: print

CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001

ISSN: 0892-6638

RECORD TYPE: Abstract LANGUAGE: English

SUMMARY LANGUAGE: English

4/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

13033028 BIOSIS NO.: 200100240177

Thiols decrease cytokine levels and down-regulate the expression of CD30 on human allergen-specific T helper (Th) 0 and Th2 cells.

AUTHOR: Bengtsson A(a); Lundberg M; Avila-Carino J; Jacobsson G; Holmgren A; Scheynius A

AUTHOR ADDRESS: (a) Department of Medicine, Unit of Clinical Allergy Research, Karolinska Hospital L2: 04, 171 76, Stockholm: asa.bengtsson@mb.ks.se**Sweden

JOURNAL: Clinical and Experimental Immunology 123 (3):p350-360 March, 2001

MEDIUM: print ISSN: 0009-9104

DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English

SUMMARY LANGUAGE: English

4/3/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

12615531 BIOSIS NO.: 200000369033

TTRAP, a novel protein that associates with CD40, tumor necrosis factor (TNF) receptor-75 and TNF receptor-associated factors (TRAFs), and that inhibits nuclear factor-kappaB activation.

AUTHOR: Pype Stefan; Declercq Wim; Ibrahimi Abdelilah; Michiels Christine; Van Rietschoten Johanna G I; Dewulf Nathalie; de Boer Mark; Vandenabeele Peter; Huylebroeck Danny(a); Remacle Jacques E

AUTHOR ADDRESS: (a) Department of Cell Growth, Differentiation and Development, Flanders Interuniversity Institute for Biotechnology, University of Leuven, Herestraat 49, Campus Gasthuisberg, B-3000, Leuven **Belgium

JOURNAL: Journal of Biological Chemistry 275 (24):p18586-18593 June 16,

```
2000
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
           (Item 6 from file: 5)
 4/3/6
DIALOG(R) File
               5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.
          BIOSIS NO.: 199800306374
11525042
Enhancement of antitumor immunity by expression of CD70 (CD27 ligand) or
  CD154 (CD40 ligand) costimulatory molecules in tumor cells.
AUTHOR: Couderc Bettina; Zitvogel Laurence; Douin-Echinard Victorine;
  Djennane Leila; Tahara Hideaki; Favre Gilles; Lotze Michael T; Robbins
  Paul D(a)
AUTHOR ADDRESS: (a) Dep. Mol. Genet. and Biochem., W1246 Biomed. Sci. Tower,
  Univ. Pittsburgh Sch. Med., Pittsburgh, **USA
JOURNAL: Cancer Gene Therapy 5 (3):p163-175 May-June, 1998
ISSN: 0929-1903
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
 4/3/7
           (Item 7 from file: 5)
DIALOG(R) File
              5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.
          BIOSIS NO.: 199800007873
11226541
CD30 ligand in lymphoma patients with CD30!+ tumors.
AUTHOR: Younes Anas(a); Consoli Ugo; Snell Virginia; Clodi Katharina;
  Kliche Kay-Oliver; Palmer J Lynn; Gruss Hans J; Armitage Richard; Thomas
  Elaine K; Cabanillas Fernando; Andreeff Michael
AUTHOR ADDRESS: (a) Dep. Hematol., Section Lymphoma, Univ. Texas M.D.
  Anderson Cancer Cent., 1515 Holcombe Blvd., Ho**USA
JOURNAL: Journal of Clinical Oncology 15 (11):p3355-3362 Nov., 1997
ISSN: 0732-183X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
           (Item 1 from file: 73)
 4/3/8
DIALOG(R) File 73: EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.
11933828
             EMBASE No: 2003044479
  T-cell costimulatory pathways relevant to transplant rejection and
tolerance
  Wells A.D.
  Dr. A.D. Wells, Dept. of Pathology/Laboratory Med., Children's Hospital
  of Philadelphia, University of Pennsylvania, 3516 Civic Center Blvd.,
  Philadelphia, PA 19104-4318 United States
  Transplantation Reviews (TRANSPL. REV.) (United States)
                                                               2002, 16/4
  (205-219)
  ISSN: 0955-470X
  DOCUMENT TYPE: Journal ; Review
  LANGUAGE: ENGLISH
```

NUMBER OF REFERENCES: 214

```
DIALOG(R) File 73: EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.
             EMBASE No: 2002021386
11449616
  Expression of CD40 ligand (CD154) in B and T lymphocytes of
Hodgkin disease: Potential therapeutic significance
  Clodi K.; Asgari Z.; Younes M.; Palmer J.L.; Cabanillas F.; Carbone A.;
Andreeff M.; Younes A.
  Dr. A. Younes, Department of Lymphoma/Myeloma, University of Texas, M. D.
  Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030
  United States
  AUTHOR EMAIL: ayounes@notes.mdacc.tmc.edu
  Cancer ( CANCER ) (United States)
                                      01 JAN 2002, 94/1 (1-5)
  CODEN: CANCA
               ISSN: 0008-543X
  DOCUMENT TYPE: Journal ; Article
  LANGUAGE: ENGLISH
                     SUMMARY LANGUAGE: ENGLISH
  NUMBER OF REFERENCES: 20
            (Item 3 from file: 73)
 4/3/10
DIALOG(R) File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.
             EMBASE No: 1999402580
07928709
  Constitutive expression and role of the TNF family ligands in apoptotic
killing of tumor cells by human NK cells
  Kashii Y.; Giorda R.; Herberman R.B.; Whiteside T.L.; Vujanovic N.L.
  Dr. N.L. Vujanovic, University of Pittsburgh, Cancer Institute,
  Biomedical Science Tower W1045, 211 Lothrop Street, Pittsburgh, PA 15213
 United States
  AUTHOR EMAIL: vujanovicn1@msx.upmc.edu
  Journal of Immunology ( J. IMMUNOL. ) (United States) 15 NOV 1999,
  163/10 (5358-5366)
                 ISSN: 0022-1767
  CODEN: JOIMA
  DOCUMENT TYPE: Journal; Article
  LANGUAGE: ENGLISH
                     SUMMARY LANGUAGE: ENGLISH
  NUMBER OF REFERENCES: 37
 4/3/11
            (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.
07068504
             EMBASE No: 1997350367
  CD30 ligand in lymphoma patients with CD30sup + tumors
  Younes A.; Consoli U.; Snell V.; Clodi K.; Kliche K.-O.; Palmer J.L.;
Gross H.J.; Armitage R.; Thomas E.K.; Cabanillas F.; Andreelf M.
  Dr. A. Younes, Department of Hematology, Section of Lymphoma, Texas M.D.
  Anderson Can. Ctr. Univ., 1515 Holcombe Blvd, Houston, TX 77030 United
  States
  AUTHOR EMAIL: ayounes@notes.mdacc.tmc.edu
  Journal of Clinical Oncology ( J. CLIN. ONCOL. ) (United States) 1997,
  15/11 (3355-3362)
                 ISSN: 0732-183X
  CODEN: JCOND
  DOCUMENT TYPE: Journal; Article
                     SUMMARY LANGUAGE: ENGLISH
  LANGUAGE: ENGLISH
  NUMBER OF REFERENCES: 24
 4/3/12
            (Item 1 from file: 399)
DIALOG(R) File 399:CA SEARCH(R)
(c) 2003 American Chemical Society. All rts. reserv.
```

4/3/9

(Item 2 from file: 73)

PATENT 138220374 CA: 138(15)220374h Anti-CD3 and anti-T cell costimulatory molecule antibodies for producing human CD4+ Th1 cells for treating infection and cancer INVENTOR (AUTHOR): Fowler, Daniel H.; Hou, Jeanne; Jung, Unsu; Gress, Ronald E.; Levine, Bruce; June, Carl LOCATION: USA ASSIGNEE: The Government of the United States of America as Represented by the Secretary of the Department of Health and Human Services; The Trustees of the University of Pennsylvania PATENT: PCT International; WO 200320904 A2 DATE: 20030313 APPLICATION: WO 2002US27824 (20020829) *US PV316854 (20010831) PAGES: 47 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-000/A DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS ; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG (Item 2 from file: 399) 4/3/13 DIALOG(R) File 399:CA SEARCH(R) (c) 2003 American Chemical Society. All rts. reserv. CA: 138(7)88660s 138088660 PATENT Monclonal anti-CD3 antibodies for producing human CD4+ Th2 cells to treat graft versus host disease, tumors, and autoimmune disorders INVENTOR(AUTHOR): Fowler, Daniel H.; Hou, Jeanne; Jung, Unsu; Gress, Ronald E.; Bishop, Michael; Levine, Bruce; June, Carl LOCATION: USA ASSIGNEE: United States of America, Health and Human Services; The Trustees of the University of Pennsylvania PATENT: PCT International ; WO 200304625 Al DATE: 20030116 APPLICATION: WO 2002US20415 (20020626) *US PV302936 (20010702) PAGES: 70 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-005/00A; C12N-005/02B; A61K-039/395B; C07K-016/00B DESIGNATED COUNTRIES: AE; AG; AL ; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW ; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG (Item 3 from file: 399) 4/3/14 DIALOG(R) File 399:CA SEARCH(R) (c) 2003 American Chemical Society. All rts. reserv. CA: 137(25)365329m PATENT 137365329 Recombinant trimerizing fusion proteins and their use in disease treatment INVENTOR (AUTHOR): Tschopp, Juerg; Schneider, Pascal LOCATION: Switz. ASSIGNEE: Apotech Research & Development Ltd. PATENT: PCT International ; WO 200290553 A2 DATE: 20021114 APPLICATION: WO 2002EP5103 (20020508) *DE 10122140 (20010508) PAGES: 46 pp. CODEN: PIXXD2 LANGUAGE: German CLASS: C12N-015/62A; C07K-014/47B; C07K-014/525B; C07K-019/00B; C12N-001/21B; C12N-005/10B;

```
A61K-038/17B DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG;
BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB;
GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR;
LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO;
RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TT; TZ; UA; UG; US; UZ; VN; YU;
ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM
; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; CH; CY; DE; DK; ES;
FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA;
GN; GQ; GW; ML; MR; NE; SN; TD; TG
 4/3/15
            (Item 4 from file: 399)
DIALOG(R) File 399:CA SEARCH(R)
(c) 2003 American Chemical Society. All rts. reserv.
  137088489
               CA: 137(7)88489x
                                   PATENT
  Secreted Frizzled-related protein (sFRP) and protein motifs that interact
with sFRP and therapeutic uses thereof
  INVENTOR(AUTHOR): Rubin, Jeffrey S.; Uren, Aykut; Horwood, Nicole Joy;
Gillespie, Matthew Todd; Kay, Brian K.; Weisblum, Bernard
  LOCATION: USA
  ASSIGNEE: The Government of the United States of America, Department of
Health and Human Services; St. Vincent's Institute of Medical Research
  PATENT: PCT International; WO 200255547 A2 DATE: 20020718
  APPLICATION: WO 2002US869 (20020110) *US PV260908 (20010110)
                 CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/00A;
  PAGES: 81 pp.
C07K-007/08B; C07K-007/06B; C12N-015/11B; A61K-038/04B; A61P-019/08B
  DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;
CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH;
GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU;
LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE;
SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZM; ZW;
AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW
; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB;
GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW;
ML; MR; NE; SN; TD; TG
            (Item 5 from file: 399)
 4/3/16
DIALOG(R) File 399:CA SEARCH(R)
(c) 2003 American Chemical Society. All rts. reserv.
               CA: 135(24)348851s
                                     PATENT
  135348851
  Albumin fusion proteins with therapeutic proteins for improved shelf-life
  INVENTOR (AUTHOR): Rosen, Craig A.; Haseltine, William A.
  LOCATION: USA
  ASSIGNEE: Human Genome Sciences, Inc
  PATENT: PCT International; WO 200179444 A2 DATE: 20011025
  APPLICATION: WO 2001US12013 (20010412) *US PV229358 (20000412) *US
PV199384 (20000425) *US PV256931 (20001221)
  PAGES: 606 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-000/A
  DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;
CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM;
HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV;
MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK;
SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ;
MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ
; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL;
PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG
```

4/3/17 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2003 American Chemical Society. All rts. reserv.

CA: 135(24)339226q PATENT 135339226 Method for treatment of tumors using photodynamic therapy INVENTOR (AUTHOR): Fanslow, William C., III; Thomas, Elaine K. LOCATION: USA ASSIGNEE: Immunex Corporation PATENT: PCT International ; WO 200180888 A2 DATE: 20011101 APPLICATION: WO 2001US13616 (20010425) *US PV199545 (20000425) PAGES: 24 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG ; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG (Item 7 from file: 399) 4/3/18 DIALOG(R) File 399:CA SEARCH(R) (c) 2003 American Chemical Society. All rts. reserv. 135104086 CA: 135(8)104086e PATENT Multimerization domain-containing fusion proteins and use of fusion protein multimers for therapy and diagnosis INVENTOR (AUTHOR): Tschopp, Juerg; Schneider, Pascal; Holler, Nils LOCATION: Switz. ASSIGNEE: Apotech Research and Development Ltd. PATENT: PCT International; WO 200149866 Al DATE: 20010712 APPLICATION: WO 2000EP13032 (20001220) *DE 19963859 (19991230) PAGES: 96 pp. CODEN: PIXXD2 LANGUAGE: German CLASS: C12N-015/62A; C12N-015/11B; C07K-014/705B; A61K-038/17B DESIGNATED COUNTRIES: AE; AG; AL ; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CR; CU; CZ; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH ; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG 4/3/19 (Item 8 from file: 399) DIALOG(R) File 399:CA SEARCH(R) (c) 2003 American Chemical Society. All rts. reserv. CA: 134(21)290751v PATENT 134290751 Recombinant single-chain receptor antagonist proteins and their use in treatment of inflammatory disorders INVENTOR (AUTHOR): Halkier, Torben; Schambye, Hans Thalsgard; Okkels, Jens Sigurd; Andersen, Kim Vilbour; Nissen, Torben Lauesgaard; Soni, Bobby; Jeppesen, Claus Bekker; Van Den Hazel, Bart LOCATION: Den. ASSIGNEE: Maxygen Aps PATENT: PCT International; WO 200125277 A1 DATE: 20010412 APPLICATION: WO 2000DK563 (20001006) *DK 991438 (19991007) *DK 991855 (19991223) *DK 20001119 (20000720) PAGES: 123 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/525A; A61K-038/22B; A61P-029/00B; C07K-019/00B; C07K-001/107B; C12N-015/62B; C07K-014/52B DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG;

SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

4/3/20 (Item 9 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2003 American Chemical Society. All rts. reserv.

134290399 CA: 134(21)290399m PATENT

Compositions and methods for tumor-targeted delivery of effector molecules

INVENTOR(AUTHOR): Bermudes, David G.; King, Ivan C.; Clairmont, Caroline
A.; Lin, Stanley L.; Belcourt, Michael

LOCATION: USA

ASSIGNEE: Vion Pharmaceuticals, Inc.

PATENT: PCT International ; WO 200125397 A2 DATE: 20010412 APPLICATION: WO 2000US23242 (20000824) *US PV157500 (19991004) *US PV157581 (19991004) *US PV157637 (19991004)

PAGES: 185 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-000/A
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;
CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR;
HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA;
MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL;
TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD;
RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG;
ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT;
SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

4/3/21 (Item 10 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2003 American Chemical Society. All rts. reserv.

133191263 CA: 133(14)191263k JOURNAL

Analysis of TNF-receptor and ligand superfamily molecules in patients with lymphoproliferative disease of granular lymphocytes

AUTHOR(S): Zambello, Renato; Trentin, Livio; Facco, Monica; Siviero, Marta; Galvan, Silvia; Piazza, Francesco; Perin, Alessandra; Agostini, Carlo; Semenzato, Gianpietro

LOCATION: Division of Hematology, Vicenza Hospital, Vicenza, Italy JOURNAL: Blood DATE: 2000 VOLUME: 96 NUMBER: 2 PAGES: 647-654 CODEN: BLOOAW ISSN: 0006-4971 LANGUAGE: English PUBLISHER: American Society of Hematology

4/3/22 (Item 11 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2003 American Chemical Society. All rts. reserv.

133163045 CA: 133(12)163045x PATENT

Preparation of human effector T cells with CD86 on their surface and their therapeutic use

INVENTOR(AUTHOR): Jeannin, Pascale; Delneste, Yves; Vittori, Marc; Bonnefoy, Jean-Yves

LOCATION: Fr.

ASSIGNEE: Pierre Fabre Medicament

PATENT: PCT International ; WO 200046352 A1 DATE: 20000810 APPLICATION: WO 2000FR240 (20000202) *FR 991187 (19990202)

PAGES: 55 pp. CODEN: PIXXD2 LANGUAGE: French CLASS: C12N-005/08A; A61P-037/00B; A61K-035/14B; C12N-005/10B; C07K-014/52B; A61K-039/00B; G01N-033/50B DESIGNATED COUNTRIES: AU; BR; CA; CN; JP; MX; US; ZA DESIGNATED REGIONAL: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT;

(c) 2003 BIOSIS. All rts. reserv.

(Item 12 from file: 399) 4/3/23 DIALOG(R) File 399:CA SEARCH(R) (c) 2003 American Chemical Society. All rts. reserv. 133145450 CA: 133(11)145450w PATENT M68: a soluble member of the tumor necrosis factor receptor family identified by gene discovery and its uses INVENTOR (AUTHOR): Bai, Chang LOCATION: USA ASSIGNEE: Merck and Co., Inc. PATENT: PCT International ; WO 200046247 A1 DATE: 20000810 APPLICATION: WO 2000US3037 (20000204) *US PV118902 (19990205) *US PV172754 (19991220) PAGES: 86 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-014/47A; C07H-021/04B; C12N-015/62B; C12N-015/63B; C12N-005/22B; G01N-033/52B; G01N-033/53B; A61K-031/70B; A61K-038/17B DESIGNATED COUNTRIES: CA; JP; US DESIGNATED REGIONAL: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE (Item 13 from file: 399) 4/3/24 DIALOG(R) File 399:CA SEARCH(R) (c) 2003 American Chemical Society. All rts. reserv. 129329705 CA: 129(25)329705g PATENT Receptor protein and its use INVENTOR (AUTHOR): Nishi, Kazunori; Shintani, Atsushi; Horiguchi, Takashi LOCATION: Japan, ASSIGNEE: Takeda Chemical Industries, Ltd. PATENT: European Pat. Appl. ; EP 873998 A2 DATE: 19981028 APPLICATION: EP 98303190 (19980424) *JP 97109798 (19970425) *JP 97251867 (19970917) PAGES: 65 pp. CODEN: EPXXDW LANGUAGE: English CLASS: C07K-014/705A; C07K-016/28B; C12N-015/12B DESIGNATED COUNTRIES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE; MC; PT; IE; SI; LT; LV; FI; RO 4/3/25 (Item 14 from file: 399) DIALOG(R) File 399:CA SEARCH(R) (c) 2003 American Chemical Society. All rts. reserv. CA: 129(7)77575f PATENT Novel expression vectors containing accessory molecule ligand genes and their use for immunomodulation and treatment of malignancies and autoimmune disease INVENTOR (AUTHOR): Kipps, Thomas J.; Sharma, Sanjai; Cantwell, Mark LOCATION: USA ASSIGNEE: University of California PATENT: PCT International; WO 9826061 A2 DATE: 19980618 APPLICATION: WO 97US22740 (19971208) *US 32145 (19961209) *US 982272 (19971201) PAGES: 167 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-015/00A; A61K-048/00B DESIGNATED COUNTRIES: AT; AU; BR; CA; CH; CN; DE; DK; ES; FI; GB; IL; JP; KR; LU; MX; NO; NZ; PT; RU; SE; SG DESIGNATED REGIONAL: AT; BE ; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE ? t s4/7/1-104/7/1 (Item 1 from file: 5) DIALOG(R) File 5:Biosis Previews(R)

13501169 BIOSIS NO.: 200200129990

Depletion of normal B-lymphocytes by rituximab therapy alters serum cytokine levels, resolves B-symptoms and induces clinical remissions in patients with relapsed classical Hodgkin's disease (HD).

AUTHOR: Younes Anas(a); Romaguera Jorge(a); Hagemeister Frederick(a); Mclaughlin Peter(a); Rodriguez Maria Alma(a); Fiumara Paolo(a); Goy Andre (a); Jeha Sima; Manning John; Medeiros L Jeffrey; Martinez Rudy F(a); Cabanillas Fernando(a)

AUTHOR ADDRESS: (a) Lymphoma/Myeloma, M.D.Anderson Cancer Center (MDACC), Houston, TX**USA

JOURNAL: Blood 98 (11 Part 1):p132a November 16, 2001

MEDIUM: print

CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001

ISSN: 0006-4971

RECORD TYPE: Abstract LANGUAGE: English

ABSTRACT: Although the malignant Hodgkin and Reed-Sternberg (H/RS) cells of HD are predominantly of B cell origin, only in 25%-30% of the cases they express CD20 antigen. However, infiltrating benign CD20-positive B cells in HD lymph nodes frequently express CD30 ligand and CD40 ligand that can provide H/RS cells with survival signals, suggesting that B-cells of HD may play a role in the growth regulation of H/RS cells in vivo. With this background, we hypothesized that depletion of the CD20-positive normal B cells from HD lesions may deprive the H/RS cells from important survival factors and could lead to clinical responses. To test this hypothesis, we initiated a pilot study of single agent rituximab for the treatment of patients with relapsed classical HD. All patients received 6 weekly doses of 375 mg/m2 rituximab. Tumor response was determined at week 9 and every 3 months thereafter. Twenty-four patients were enrolled, of whom 22 patients are evaluable for treatment response. All patients had nodular sclerosis histology. Median number of prior treatment regimens was 4 (range 2 to 12), and 18 patients had prior bone marrow or stem cell tranplantation. Relapses involved extranodal sites in 12 patients. CD20 expression on H/RS was observed in 5 cases. Five (23%) patients achieved partial or complete remissions (2 expressed CD20 on H/RS cells), and 8 (36%) had stable disease. All responses were seen in patients whose disease did not involve extranodal sites and were irrespective of CD20 expression on H/RS cells. Seven patients had B symptoms prior to rituximab therapy, which resolved in 6 after therapy (3 had also had clinical esponses). Serum levels of IL-6, IL-10, IL-12, IL-13, and interferon-gamma were measured in 8 patients before and after rituximab therapy by ELISA. Rituximab therapy significantly decreased IL-6 levels in 2 patients who also achieved partial remissions. IL-10 levels decreased in 3 patients but did not correlate with clinical responses. None of the patients had detectable levels of serum IL-12, interferon-gamma, or IL-13. Our data suggest that depletion of normal B cells in patients with relapsed classical HD can alter cytokine levels, improve B-symptoms, and may result in clinical remissions esppecially in patients whose disease is limited to the lymph nodes. Based on these data we are currently combining rituximab with chemotherapy for the treatment of patients with classical HD to explore whether depletion of normal B cells from HD lesions may enhance the activity of chemotherapy.

4/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

13112983 BIOSIS NO.: 200100320132

A pilot study of rituximab in patients with relapsed Hodgkin's disease of classical type.

AUTHOR: Younes A(a); Romaguera J(a); Hagemeister F(a); Rodriguez M(a); McLaughlin P(a); Medeiros J(a); Cabanillas F(a)

AUTHOR ADDRESS: (a)U.T. M.D. Anderson Cancer Center, Houston, TX**USA

JOURNAL: Blood 96 (11 Part 1):p733a November 16, 2000

MEDIUM: print

CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000

SPONSOR: American Society of Hematology

ISSN: 0006-4971 RECORD TYPE: Abstract LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: We have previously reported that normal B lymphocytes in lymph nodes and peripheral blood of patients with Hodgkin's disease (HD) express CD40 Ligand (CD40L) and CD30 Ligand (CD30L). Both ligands can activate NF-kappabeta and promote Reed-Sternberg (RS) cell survival. Therefore, we hypothesized that elimination of B lymphocytes from HD lesions may deprive the RS cells of important growth signals and may result in tumor regression. To examine this hypothesis, we treated patients with relapsed classic HD with 375 mg/m2 of rituximab IV every week for 6 consecutive weeks. Patients were eligible if they had relapsed classic HD, regardless of CD20 antigen expression on RS cells, and had at least two prior treatment regimens. Patients were excluded if they were pregnant women, had lymphocyte depletion or lymphocyte-predominant histology, were infected with HIV virus, or had CNS involvement by lymphoma. Objective tumor response was assessed after completion of six doses. Eighteen patients with nodular sclerosis histology are enrolled, of whom 15 have completed the planned therapy and are evaluable for response. CD20 antigen was expressed by the RS cells in 5 patients. Patient age ranged between 17 and 66 years and the number of prior treatment regimens ranged between 2 and 7 (median, 5 regimens). Thirteen patients had prior bone marrow transplantation. Seven patients had disease limited to lymph nodes and 8 had disease involving lymph nodes plus lungs and/or liver. Three patients (20%) had major responses (2 PRs and 1 CRu). All responding patients had disease limited to lymph nodes and the RS cells did not express CD20. Six additional patients had stable disease of whom 2 experienced resolution of B symptoms. We conclude that rituximab therapy, possibly by eliminating normal B lymphocytes from HD patients, can result in major clinical responses and symptom improvement.

4/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

13057538 BIOSIS NO.: 200100264687

Chronic lymphocytic leukemia B cells impair immunoglobulin class switching by inducing CD30+ suppressor T cells.

AUTHOR: Cerutti Andrea(a); Kim Edmund C(a); Zan Hong(a); Schaffer Andras(a); Casali Paolo(a)

AUTHOR ADDRESS: (a) Weill Medical College of Cornell University, 1300 York Avenue, New York, NY, 10021**USA

JOURNAL: FASEB Journal 15 (5):pA1202 March 8, 2001

MEDIUM: print

CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001

ISSN: 0892-6638

RECORD TYPE: Abstract LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: B cell chronic lymphocytic leukemia (CLL) is a chronic lymphoproliferative disorder associated with impaired Ig class switching from IgM to IgG and IgA, a defect that leads to recurrent infections. The pathogenesis of this immunodeficiency is poorly understood. Naive B cells undergo class switching upon engagement of CD40 by CD154 (CD40 ligand), a molecule expressed by T cells a few hours after activation by antigen. Four days later, T cells express CD30, a negative modulator of the immune response. We show here that leukemic CLL B cells rapidly up-regulate T cell CD30 through a CD134 ligand (OX40 ligand) and IL-4-dependent mechanism. These CD30+ T cells inhibit class switch DNA recombination by engaging CD153 (CD30 ligand), a molecule that interferes with the assembly of the CD40:tumor necrosis factor receptor associated factor (TRAF) complex in CD154-activated naive B cells. By showing that engagement of T cell CD30 by CD153 on leukemic B cells down-regulates CD154, our findings suggest that, in CLL, dysregulated CD30:CD153 interaction impairs class switching by transmitting bidirectional CD40 and CD154-inhibitory signals.

4/7/4 (Item 4 from file: 5) DIALOG(R) File 5:Biosis Previews(R) (c) 2003 BIOSIS. All rts. reserv. 13033028 BIOSIS NO.: 200100240177 Thiols decrease cytokine levels and down-regulate the expression of CD30 on human allergen-specific T helper (Th) 0 and Th2 cells. AUTHOR: Bengtsson A(a); Lundberg M; Avila-Carino J; Jacobsson G; Holmgren A ; Scheynius A AUTHOR ADDRESS: (a) Department of Medicine, Unit of Clinical Allergy Research, Karolinska Hospital L2: 04, 171 76, Stockholm: asa.bengtsson@mb.ks.se**Sweden JOURNAL: Clinical and Experimental Immunology 123 (3):p350-360 March, 2001 MEDIUM: print ISSN: 0009-9104 DOCUMENT TYPE: Article

RECORD TYPE: Abstract LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: The thiol antioxidant N-acetyl-L-cysteine (NAC), known as a precursor of glutathione (GSH), is used in AIDS treatment trials, as a chemoprotectant in cancer chemotherapy and in treatment of chronic bronchitis. In vitro, GSH and NAC are known to enhance T cell proliferation, production of IL-2 and up-regulation of the IL-2 receptor. The 120-kD CD30 surface antigen belongs to the tumour necrosis factor (TNF) receptor superfamily. It is expressed by activated T helper (Th) cells and its expression is sustained in Th2 cells. We have analysed the effect of GSH and NAC on the cytokine profile and CD30 expression on human allergen-specific T cell clones (TCC). TCC were stimulated with anti-CD3 antibodies in the presence of different concentrations of GSH and NAC. Both thiols caused a dose dependent down-regulation of IL-4, IL-5 and IFN-gamma levels in Th0 and Th2 clones, with the most pronounced decrease of IL-4. Furthermore, they down-regulated the surface expression of CD30, and the levels of soluble CD30 (sCD30) in the culture supernatants were decreased. In contrast, the surface expression of CD28 or CD40 ligand (CD40L) was not significantly changed after treatment with 20 mM NAC. These results indicate that GSH and NAC favour a Th1 response by a preferential down-regulation of IL-4. In addition, the expression of CD30 was down regulated by GSH and NAC, suggesting that CD30 expression is dependent on IL-4, or modified by NAC. In the likely event that CD30 and its soluble counterpart prove to contribute to the pathogenesis in Th2 related diseases such as allergy, NAC may be

considered as a future therapeutic agent in the treatment of these diseases.

4/7/5 (Item 5 from file: 5) DIALOG(R) File 5:Biosis Previews(R) (c) 2003 BIOSIS. All rts. reserv. BIOSIS NO.: 200000369033 12615531 TTRAP, a novel protein that associates with CD40, tumor necrosis factor (TNF) receptor-75 and TNF receptor-associated factors (TRAFs), and that inhibits nuclear factor-kappaB activation. AUTHOR: Pype Stefan; Declercq Wim; Ibrahimi Abdelilah; Michiels Christine; Van Rietschoten Johanna G I; Dewulf Nathalie; de Boer Mark; Vandenabeele Peter; Huylebroeck Danny(a); Remacle Jacques E AUTHOR ADDRESS: (a) Department of Cell Growth, Differentiation and Development, Flanders Interuniversity Institute for Biotechnology, University of Leuven, Herestraat 49, Campus Gasthuisberg, B-3000, Leuven **Belgium JOURNAL: Journal of Biological Chemistry 275 (24):p18586-18593 June 16, MEDIUM: print ISSN: 0021-9258 DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English SUMMARY LANGUAGE: English ABSTRACT: CD40 belongs to the tumor necrosis factor (TNF) receptor family. CD40 signaling involves the recruitment of TNF receptor-associated factors (TRAFs) to its cytoplasmic domain. We have identified a novel

intracellular CD40-binding protein termed TRAF and TNF receptor-associated protein (TTRAP) that also interacts with TNF-R75 and CD30. The region of the CD40 cytoplasmic domain that is required for TTRAP association overlaps with the TRAF6 recognition motif. Association of TTRAP with CD40 increases profoundly in response to treatment of cells with CD40L. Interestingly, TTRAP also associates with TRAFs, with the highest affinity for TRAF6. In transfected cells, TTRAP inhibits in a dose- dependent manner the transcriptional activation of a nuclear factor-kappaB (NF-kappaB)-dependent reporter mediated by CD40, TNF-R75 or Phorbol 12-myristate 13-acetate (PMA) and to a lesser extent by TRAF2, TRAF6, TNF-alpha, or interleukin-1beta (IL-1beta). TTRAP does not affect stimulation of NF-kappaB induced by overexpression of the NF-kappaB-inducing kinase (NIK), the IkappaB kinase alpha (IKKalpha), or the NF-kappaB subunit P65/RelA, suggesting it acts upstream of the latter proteins. Our results indicate that we have isolated a novel regulatory factor that is involved in signal transduction by distinct members of the TNF receptor family.

4/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

11525042 BIOSIS NO.: 199800306374
Enhancement of antitumor immunity by expression of CD70 (CD27 ligand) or CD154 (CD40 ligand) costimulatory molecules in tumor cells.
AUTHOR: Couderc Bettina; Zitvogel Laurence; Douin-Echinard Victorine; Djennane Leila; Tahara Hideaki; Favre Gilles; Lotze Michael T; Robbins Paul D(a)
AUTHOR ADDRESS: (a)Dep. Mol. Genet. and Biochem., W1246 Biomed. Sci. Tower, Univ. Pittsburgh Sch. Med., Pittsburgh,**USA
JOURNAL: Cancer Gene Therapy 5 (3):p163-175 May-June, 1998
ISSN: 0929-1903

DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English

ABSTRACT: CD70 (CD27 ligand (CD27L)), CD153 (CD30L), and CD154 (CD40L) are members of the tumor necrosis factor family of costimulatory molecules and expressed on the surface of T cells that are important for both T- and B-cell help. We examined the capacity for expression of these tumor necrosis factor family members on tumor cells to induce an antitumor response either in the presence or absence of interleukin 12. Retroviral vectors were constructed that expressed high levels of membrane bound CD70, CD153, or CD154 following infection and selection of the murine tumor lines MCA 207 or TS/A. The genetically modified tumor cells expressing these molecules were able to stimulate splenic cell proliferation, demonstrating that the expressed costimulatory molecules were biologically active. When tested for tumor establishment, the expression of either CD70 or CD154 was able to slow tumor growth. Similarly, CD70 or CD154 were able to induce antitumor immunity at a higher frequency when tested in vaccination and therapy models. CD70 was able to induce antitumor immunity at a level similar to CD80 when tested either in the presence or absence of interleukin 12. Moreover, coexpression of CD70 and CD80 was able to synergize the induction of a higher frequency of antitumor immunity in a vaccination model. Taken together, our results suggest that CD154 and in particular CD70 are able to contribute to the induction of the immune response to tumor in murine models and thus may be of use for human clinical trials.

4/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

11226541 BIOSIS NO.: 199800007873

CD30 ligand in lymphoma patients with CD30!+ tumors.

AUTHOR: Younes Anas(a); Consoli Ugo; Snell Virginia; Clodi Katharina; Kliche Kay-Oliver; Palmer J Lynn; Gruss Hans J; Armitage Richard; Thomas Elaine K; Cabanillas Fernando; Andreeff Michael

AUTHOR ADDRESS: (a) Dep. Hematol., Section Lymphoma, Univ. Texas M.D. Anderson Cancer Cent., 1515 Holcombe Blvd., Ho**USA

JOURNAL: Journal of Clinical Oncology 15 (11):p3355-3362 Nov., 1997

ISSN: 0732-183X

DOCUMENT TYPE: Article RECORD TYPE: Abstract LANGUAGE: English

ABSTRACT: Purpose: CD30 ligand (CD30L), which is expressed on resting B and activated T lymphocytes, can induce cell death in several CD30!+ cell lines. Patients with CD30!+ tumors (Hodgkin's disease and Ki-1!+ non-Hodgkin's lymphoma) frequently have elevated soluble CD30 (sCD30) levels in their serum, which correlates with a poor prognosis. The role of sCD30 in protecting tumor cells from CD30L-mediated cell death and the pattern of CD30L expression on human peripheral-blood lymphocytes (PBLs) of normal donors and patients with CD30!+ tumors are investigated. Materials and Methods: CD30L surface protein expression was determined by two-color flow cytometry on PBLs of patients with CD30!+ tumors and normal individuals. CD30L levels were determined on subsets of PBLs before and after stimulation with phytohemagglutinin (PHA), anti-CD3 antibody, or CD40L. sCD30 was measured by enzyme-linked immunosorbent assay (ELISA). The apoptotic activity of membrane-bound CD30L was tested in a CD30!+ cell line by the annexin V-binding method. Results: Unstimulated T lymphocytes of normal donors and patients with lymphoma rarely expressed CD30L surface protein,

but were able to express it after stimulation with PHA or anti-CD3 antibody. Resting B cells of patients with CD30!+ tumors had lower levels of detectable surface CD30L compared with normal donors (mean, 55% and 80.6%, respectively; P = .0008). Patients with high levels of serum sCD30 had lower detectable levels of CD30L on their PBLs (R!2 = .72, P = .0008) and exogenous sCD30 blocked membrane-bound CD30L-mediated apoptosis in a CD30!+ cell line. Conclusion:

In patients with CD30!+ tumors, sCD30 can decrease the availability of CD30L on PBLs. Blocking the apoptosis-inducing activity of CD30L by its soluble receptor may explain how CD30!+ tumors escape immunosurveillance and may be related to the reported poor prognosis of patients who have elevated sCD30 levels.

4/7/8 (Item 1 from file: 73) DIALOG(R) File 73:EMBASE (c) 2003 Elsevier Science B.V. All rts. reserv. 11933828 EMBASE No: 2003044479 T-cell costimulatory pathways relevant to transplant rejection and tolerance Wells A.D. Dr. A.D. Wells, Dept. of Pathology/Laboratory Med., Children's Hospital of Philadelphia, University of Pennsylvania, 3516 Civic Center Blvd., Philadelphia, PA 19104-4318 United States Transplantation Reviews (TRANSPL. REV.) (United States) (205-219)ISSN: 0955-470X DOCUMENT TYPE: Journal ; Review LANGUAGE: ENGLISH NUMBER OF REFERENCES: 214 4/7/9 (Item 2 from file: 73) DIALOG(R) File 73:EMBASE (c) 2003 Elsevier Science B.V. All rts. reserv. 11449616 EMBASE No: 2002021386 Expression of CD40 ligand (CD154) in B and T lymphocytes of Hodgkin disease: Potential therapeutic significance Clodi K.; Asgari Z.; Younes M.; Palmer J.L.; Cabanillas F.; Carbone A.; Andreeff M.; Younes A. Dr. A. Younes, Department of Lymphoma/Myeloma, University of Texas, M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030 United States AUTHOR EMAIL: ayounes@notes.mdacc.tmc.edu Cancer (CANCER) (United States) 01 JAN 2002, 94/1 (1-5) CODEN: CANCA ISSN: 0008-543X DOCUMENT TYPE: Journal ; Article LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH NUMBER OF REFERENCES: 20

BACKGROUND. The malignant Hodgkin and Reed-Sternberg (H/RS) cells of Hodgkin disease (HD) express CD30 and CD40 receptors that can activate nuclear factor kappa B and transduce survival signals. The authors have reported previously that the B lymphocytes of HD express CD30 ligand (CD30L, CD153). Furthermore, they and others have reported previously that the CD40L survival pathway is augmented in patients with B-cell malignancies, as CD40L was constitutively expressed by the malignant B cells and infiltrating T cells, and sera from those patients contained elevated levels of soluble CD40L. In this study, the authors investigated the hypothesis that the survival of H/RS cells was similarly promoted by an augmented CD40L signals in HD patients.

METHODS. The expression of CD40L on lymphocyte subsets of patients with classic HD was determined by two-color fluorescent-activated cell sorter analysis. Serum soluble CD40L levels were determined by enzyme linked immunosorbent assay. RESULTS. CD40L was constitutively expressed on both the T and B cells of HD patients but was more prominently expressed on the B lymphocytes. Soluble CD40L was detected in the serum of 17 of 37 patients (45%) and was higher than 1 ng/mL in 4 patients (10%). Both interleukin (IL)-4 and IL-10, which are known to be secreted by H/RS cells and surrounding T cells, up-regulated CD40L expression on normal B cells. CONCLUSIONS. Thus, the expression of CD40L and CD30L on the B cells of HD patients suggests that B lymphocytes may play a role in the regulation of H/RS cell growth in vivo. Depriving H/RS cells from CD30L and CD40L survival signals by eliminating B cells from HD lesions may be of therapeutic value. (c) 2002 American Cancer Society.

```
(Item 3 from file: 73)
 4/7/10
DIALOG(R) File 73: EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.
07928709
             EMBASE No: 1999402580
  Constitutive expression and role of the TNF family ligands in apoptotic
killing of tumor cells by human NK cells
  Kashii Y.; Giorda R.; Herberman R.B.; Whiteside T.L.; Vujanovic N.L.
  Dr. N.L. Vujanovic, University of Pittsburgh, Cancer Institute,
  Biomedical Science Tower W1045, 211 Lothrop Street, Pittsburgh, PA 15213
 United States
  AUTHOR EMAIL: vujanovicn1@msx.upmc.edu
  Journal of Immunology ( J. IMMUNOL. ) (United States) 15 NOV 1999,
  163/10 (5358-5366)
  CODEN: JOIMA
                 ISSN: 0022-1767
  DOCUMENT TYPE: Journal; Article
  LANGUAGE: ENGLISH
                     SUMMARY LANGUAGE: ENGLISH
  NUMBER OF REFERENCES: 37
```

Natural killer cells mediate spontaneously secretory/necrotic killing against rare leukemia cell lines and a nonsecretory/apoptotic killing against a large variety of tumor cell lines. The molecules involved in nonsecretory/apoptotic killing are largely undefined. In the present study, freshly isolated, nonactivated, human NK cells were shown to express TNF, lymphotoxin (LT)-alpha, LT-beta, Fas ligand (L), CD27L, CD30L, OX40L, 4-1BBL, and TNF-related apoptosis-inducing ligand (TRAIL), but not CD40L or nerve growth factor. Complementary receptors were demonstrated to be expressed on the cell surface of solid tumor cell lines susceptible to apoptotic killing mediated by NK cells. Individually applied, antagonists of TNF, LT-alphainf 1Binf 2, or FasL fully inhibited NK cell-mediated apoptotic killing of tumor cells. On the other hand, recombinant TNF, LT-alphainf 1Binf 2, or FasL applied individually or as pairs were not cytotoxic. In contrast, a mixture of the three ligands mediated significant apoptosis in tumor cells. These findings demonstrate that human NK cells constitutively express several of the TNF family ligands and induce apoptosis in tumor cells by simultaneous engagement of at least three of these cytotoxic molecules. ? t s4/kwic/24,25 >>>KWIC option is not available in file(s): 399 ? ds

```
Set Items Description
S1 745 (CD40L OR CD40(W)LIGAND) AND (TREAT? OR THERAP? OR PREVENT?
OR SUPPRESS? OR BLOCK? OR INHIBIT?)(20N)(CANCER? OR TUMOR? OR TUMOUR?)
S2 1 S1 AND PHOTODYNAMIC
```

S3 33 S1 AND CD30?